BIOMARKERS OF CADMIUM EXPOSURE

Cadmium is a cumulative toxin with a biological half-life of over 10 years in man. In blood, over 70% of the cadmium is bound to red blood cells. In non-occupationally exposed adults, cadmium levels in blood are usually below 1 µg/100 mL whole blood (median value around 0.15). Current cadmium detection limit in blood and urine is .02 µg/L.

Cadmium accumulates mainly in the kidney and in the liver, with about 50% of the body burden found in these two organs. Estimates of the average body burden of non-occupationally exposed adults range from 5 to 40 mg. The body burden of smokers is about twice that of non-smokers. In all tissues, cadmium is bound mainly to metallothionein. The metal is mainly excreted via the urine and the extent of urinary excretion increases with age. In adults not occupationally exposed to the metal, the level in urine is usually below 2 µg Cd/g creatinine. Cadmium can also be excreted by other routes (bile, gastrointestinal tract, saliva, hair, nails), but to a lesser extent than in urine. In man, the two main target organs after long-term exposure to cadmium are the lung and the kidney, though it is generally accepted that the kidney is the critical organ (i.e., the organ that exhibits the first adverse effect). The first detectable adverse effect of cadmium on the kidney is an increased excretion of specific proteins in urine.

Several approaches have been used to evaluate the critical internal dose of cadmium, the dose that under chronic exposure conditions may lead to the occurrence of adverse functional changes in the kidney. It is now possible to measure directly by neutron activation the amount of the metal that has accumulated in the two mains sites of deposition, i.e., the liver and the kidney. However, the evaluation of tissue cadmium in vivo by neutron activation is not a routine procedure. Therefore, it is important to evaluate to what extent indirect biological indicators, such as cadmium levels in blood and urine or metallothionein levels in plasma and urine can be used to estimate the internal dose.

The significance of cadmium in urine can be summarized as follows. At low exposure conditions (i.e., general environmental exposure or moderate occupational exposure), when the total amount of cadmium absorbed has not yet saturated all the available cadmium binding sites in the organism (in particular the kidney), the cadmium concentration in urine reflects mainly the cadmium level in the body and hence in the kidney. When integrated exposure has been so high as to cause a saturation of the binding sites, cadmium in urine may then be related partly to the body burden and partly to the recent exposure. The relative importance of each factor depends on the intensity of exposure. Thus, in workers newly exposed to cadmium, a time lag is observed before cadmium in urine correlates with exposure. This time interval will depend on the intensity of the integrated exposure to cadmium. It is also known that when renal dysfunction occurs the loss of cadmium from the organism (probably from the kidney)

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increases. Recent advances permit accurate determinations of cadmium in as little as 1 ml of blood or urine.

In urine, cadmium is present mainly bound to metallothionein. Hence, the determination of the level of this protein in urine may provide the same information as the determination of cadmium, but metallothionein analysis presents an advantage over cadmium analysis in that it is not subject to external contamination. A radioimmunoassay has been developed for the determination of metallothionein in urine. Sufficient information is not available to propose, however, a biological threshold limit value for this parameter applicable to workers without kidney dysfunction.

With regard to the significance of the cadmium level in blood, several arguments based on human observations and animal experiments suggest that it reflects mainly the last few months of exposure. Further studies are necessary to validate the biological significance of the metallothionein level in plasma.

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